Homogeneous Hydrogenation of Methyl Linolenate Catalyzed by Platinum–Tin Complexes[1]

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Methyl linolenate was hydrogenated at 500 psi in the presence of chloroplatinic acid, hydridochlorobis(triphenylphosphine)platinum(II), and dichlorobis(triphenylarsine)platinum(II), each in mixture with stannous chloride in methanol–benzene solution. Dienes and monoenes were formed as major products. Conjugated dienetrienes and conjugated trienes were important initial and intermediate products. No stearate was formed. With the bimetallic complex, trichlorotin–hydridobis(triphenylphosphine)platinum(II), conversion of linolenate into conjugated dienetrienes was the major reaction. In pure methanol solution, homogeneous hydrogenation with chloroplatinic acid and stannous chloride occurred at atmospheric pressure. Although at 30° considerable conjugation of linolenate occurred, at 40° the hydrogenation was highly selective for the formation of diene. The mechanism advanced for the homogeneous hydrogenation involves initial conjugation through platinum–tin–diene adducts. Hydrogenation of the intermediate conjugated dienetrienes and conjugated trienes produces a mixture of isomeric *trans* monoenes and dienes. Formation of unreactive dienes with double bonds separated by several methylene groups accounts for the high selectivity of these platinum–tin catalysts for the formation of dienes from methyl linolenate.

Previous studies at the Northern Regional Research Laboratory have shown that polyunsaturated fatty esters were selectively hydrogenated with various soluble organometallic complexes.[3] Cramer, *et al.*,[4] reported that a complex from a mixture of chloroplatinic acid and stannous chloride is an effective homogeneous catalyst for the hydrogenation of ethylene and acetylene at room temperature and atmospheric pressure. More recently, studies at the University of Illinois[5] have revealed that soybean oil methyl esters were also hydrogenated with this platinum–tin chloride catalyst and various soluble triphenylphosphine derivatives of platinum(II) complexes in the presence of stannous chloride under hydrogen pressure. These catalysts were selective in that reduction stopped at the monoene stage. Methyl linoleate was conjugated and hydrogenated to *trans*-monoene, and methyl oleate was extensively isomerized to the *trans* configuration.

This paper reports related studies on the hydrogenation of methyl linolenate. The course of the reaction was followed and the isomeric reduction products were characterized in detail to elucidate the mechanism of homogeneous hydrogenation.

Results

Methyl linolenate was effectively hydrogenated at 500 psi with mixtures of triphenylphosphine or triphenylarsine derivatives of platinum(II) or chloroplatinic acid with stannous chloride. Typical rate curves are shown in Figure 1. The mixture (hydridochlorobis(triphenylphosphine)platinum(II) and stannous chloride formed conjugated dienetrienes (trienes with two double bonds conjugated and one isolated) and conjugated trienes as important initial products (Figure 1A). These conjugated products were then reduced to conjugated and unconjugated dienes and monoenes. No stearate was formed. Rate curves were similar for the hydrogenation catalyzed with a mixture of dichlorobis(triphenylarsine)platinum(II) and stannous chloride, which is a more active catalyst than hydridochlorobis(triphenylphosphine)platinum(II) and stannous chloride (Figure 1B). Conjugated dienetrienes were again primary initial products, but they were rapidly reduced to give dienes as the main reduction products followed by monoenes. When hydrogenations were carried out with the same two catalysts but at 65°, appreciable isomerization of methyl linolenate occurred to give conjugated dienetrienes as major products and conjugated trienes as minor products. Reduction to dienes was small.

The expected complex involved in the reduction with the triphenylphosphineplatinum and stannous chloride was synthesized as the trichlorotin–hydridobis(triphenylphosphine)platinum(II). With this bimetallic complex, conjugation of linolenate to conjugated dienetrienes was the most important reaction (Figure 1C). Minor products include conjugated and unconjugated dienes and conjugated trienes. Analyses of the final reaction mixtures (runs 1–3) by infrared gave values for isolated *trans* ranging from 57 to 78% expressed as methyl elaidate. The unsaturated products were therefore largely in the *trans* configuration.

The complex from mixtures of chloroplatinic acid and stannous chloride was more active as a hydrogenation catalyst than were the triphenylphosphine and triphenylarsine derivatives of platinum. This mixture was also most selective for the formation of dienes as the main hydrogenation products from linolenate (Figure 1D). Conjugated dienetrienes were still major initial products. Minor products include monoene, conjugated dienes, and conjugated trienes. Compositional data in Table IA show that at 65° considerable reduction occurred to give dienes as major products and some monoenes. At 100° and smaller catalyst concen-

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(3) (a) E. A. Emken, E. N. Frankel, and R. O. Butterfield, *J. Am. Oil Chemists' Soc.*, **43**, 14 (1966); (b) E. N. Frankel, E. A. Emken, and V. L. Davison, *J. Org. Chem.*, **30**, 2739 (1965); (c) E. N. Frankel, E. A. Emken, H. M. Peters, V. L. Davison, and R. O. Butterfield, *ibid.*, **29**, 3292 (1964); (d) E. N. Frankel, E. P. Jones, V. L. Davison, E. A. Emken, and H. J. Dutton, *J. Am. Oil Chemists' Soc.*, **42**, 130 (1965); (e) E. N. Frankel, H. M. Peters, E. P. Jones, and H. J. Dutton, *ibid.*, **41**, 186 (1964).

(4) R. D. Cramer, E. L. Jenner, R. V. Lindsey, Jr., and U. G. Stolberg, *J. Am. Chem. Soc.*, **85**, 1691 (1963).

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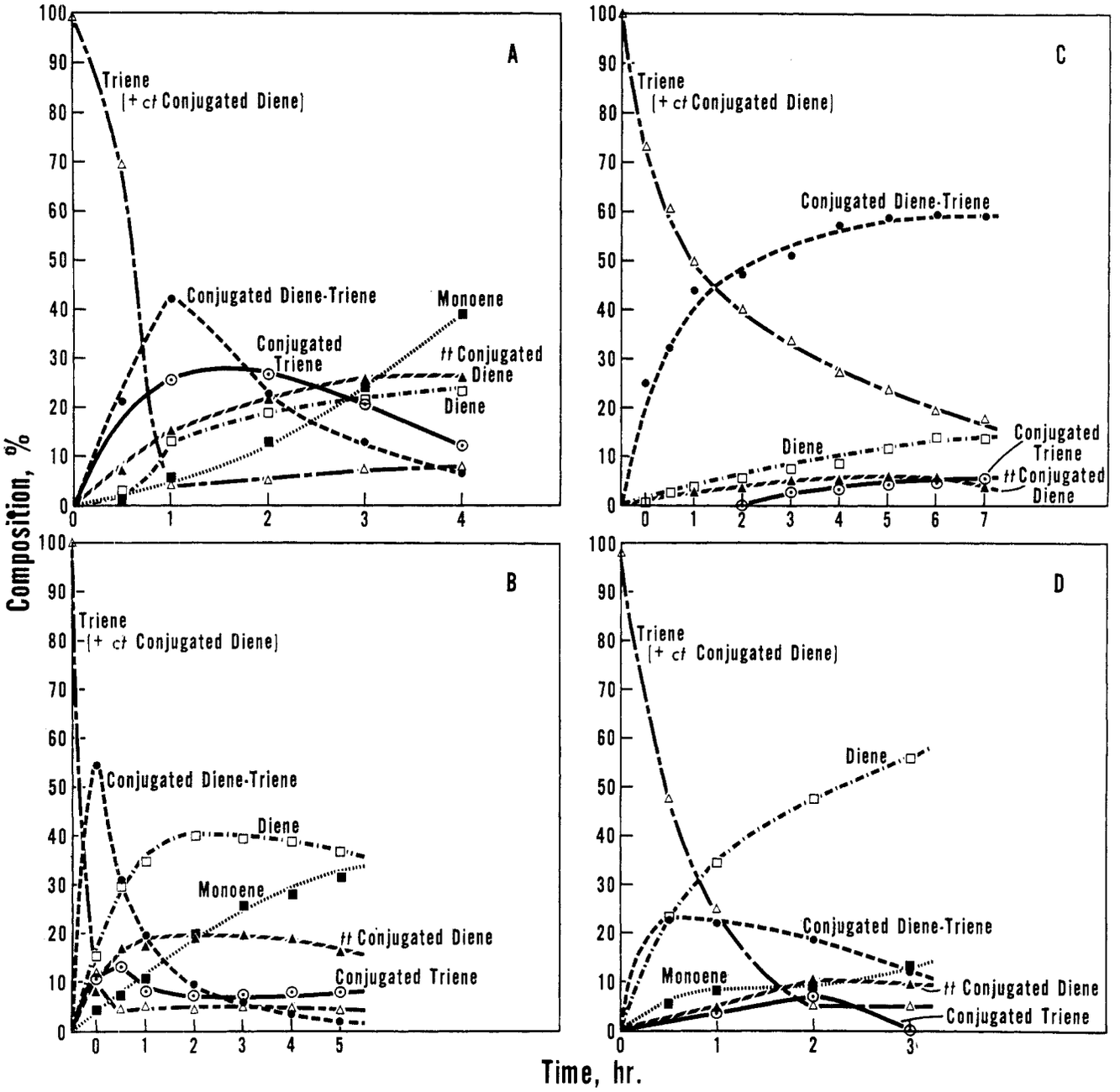

Figure 1.—Rate of hydrogenation of methyl linolenate catalyzed by platinum–tin complexes at 500-psi H_2 pressure in methanol–benzene (40:60%) solution: A, hydridochlorobis(triphenylphosphine)platinum(II) + stannous chloride, run 1 (100°); B, dichlorobis-(triphenylarsine)platinum(II) + stannous chloride, run 2 (100°); C, (trichlorotin–hydridobis(triphenylphosphine)platinum(II), run 3 (100°); and D, chloroplatinic acid + stannous chloride, run 5 (65°) [see Table IA (footnotes *c* and *d*)].

trations the selectivity of hydrogenation increased to give high proportions of dienes, some conjugated dienetrienes, but very little monoenes.

The effect of methanol concentration in the reaction mixtures was also studied. Increasing the proportion of methanol accelerated the rate of conjugation. When pure methanol was used as solvent, methyl linolenate could be hydrogenated at atmospheric pressure but with higher concentrations of catalyst (Table IB). At 30° the reduction was highly selective for the production of diene, but considerable conjugation occurred (conjugated dienetrienes). At 40° less conjugation was observed, and the reduction was still more selective toward diene formation.

Hydrogenated products of methyl linolenate were separated by countercurrent distribution. Analysis of the monoene fractions (Table II) shows 72–77% isolated *trans* unsaturation. The diene fraction from reduction with hydrochlorobis(triphenylphosphine)platinum-(II) and stannous chloride was 66% conjugated predominantly in the *trans,trans* configuration as determined by gas–liquid partition chromatography (glpc) and infrared ($a_{10.1\,\mu}/a_{10.6\,\mu}$). The remainder of the diene fraction was unconjugatable with alkali; therefore, the double bonds are separated by more than one methylene group. Infrared analysis showed approximately one-half isolated *trans* double bond per diene molecule. The diene from reduction with chloroplatinic acid and stannous chloride was initially less conjugated, was 18% conjugatable with alkali, and had more than one *trans* isolated double bond. The triene fractions from both hydrogenated products were a mixture of con-

TABLE I

HYDROGENATION OF METHYL LINOLENATE WITH CHLOROPLATINIC ACID PLUS STANNOUS CHLORIDE (1:10 *M*)

Run	Conditions: Catalyst concn, *M*[b]	Temp, °C	Time, hr	Composition,[a] %: Monoene	Unconjd diene	Triene + *ct*-conjd diene[c]	*tt*-Conjd diene[d]	Conjd diene-triene	Conjd triene
				A. Pressure Hydrogenation[e]					
4	0.025	65	6	0.3	6.6	60.0	15.6	17.5	...
5	0.050	65	3	13.2	59.4	5.2	9.7	12.5	...
6	0.10	65	3	32.4	64.0	0.6	1.8	1.2	...
7	0.025	100	6	0.5	10.0	66.2	9.9	13.4	...
8	0.050	100	3	7.7	51.8	5.9	8.5	26.1	...
				B. Atmospheric Hydrogenation[f]					
9	0.10	30	5	0.3	8.1	23.1	10.7	42.5	15.4
10	0.20	30	5	1.0	24.2	11.1	13.2	48.4	2.1
11	0.40	30	5	1.2	31.9	5.3	9.6	47.2	4.7
12	0.10	40	5	2.8	47.1	37.8	...	11.5	0.8
13	0.2	40	5	5.9	66.4	4.5	5.3	15.9	2.0

[a] Determined by glpc on final reaction products. [b] Per mole of methyl linolenate. [c] Triene and *cis,trans*- (*ct*-) conjugated diene were not separated by glpc. [d] *tt* = *trans,trans*. [e] 500-psi H_2 pressure in methanol–benzene (40:60%) solution. [f] Atmospheric H_2 pressure in pure methanol solution.

TABLE II

ANALYSES[a] OF COUNTERCURRENT DISTRIBUTION FRACTIONS FROM HYDROGENATED METHYL LINOLENATE[b]

	Run 1[c]: Monoene	Diene	Triene	Run 5[d]: Monoene	Diene	Triene
			Glpc, %			
Monoene	100	0.3	...	100	0.0	...
Unconjugated diene	...	33.7	...	...	85.2	...
Conjugated diene						
cis,trans	...	16.4	...	...	5.3	...
trans,trans	...	49.6	...	...	9.5	...
Triene	...	...	0.0	...	...	3.2
Conjugated dienetriene	...	...	44.2	...	...	89.0
Conjugated triene	...	...	55.8	...	...	7.8
			Infrared			
Isolated *trans*[e]	76.8	49.5	42.7	71.6	129.3	77.7
$a_{10.1\ \mu}$	...	0.56	0.87	...	0.19	0.38
$a_{10.6\ \mu}$	...	0.06	...	...	...	0.14
			Ultraviolet			
$a_{230\ m\mu}$	...	60.4	59.4	...	19.0	62.5
$a_{268\ m\mu}$	...	...	106.9	...	...	17.7
			Alkali conjugation			
Diene[f]	...	0	9.6	...	18.2	...
Triene[g]	...	...	18.0	...	...	...

[a] Carried out on center cuts of each fraction. [b] Fractionations carried out on final reaction products. [c] See Figure 1. [d] See Table IA. [e] Expressed as methyl elaidate. [f] Calculated as follows: diene = $a_{230\ m\mu}$ after alkali − $a_{230\ m\mu}$ before alkali/$a_{230\ m\mu}$ after alkali (pure linoleate). [g] Calculated as the diene was, but $a_{266\ m\mu}$ values were used for the triene values.

jugated dienetrienes and conjugated trienes as was shown by glpc and ultraviolet. Analyses by infrared indicated that the isolated double bond of the conjugated denetrienes was largely in the *trans* configuration and that the conjugated diene system had a *trans,trans* configuration ($a_{10.1\mu}$).

The double-bond distribution in *cis*- and *trans*-monoene fractions determined by potassium permanganate–potassium periodate oxidative cleavage is shown in Figure 2. The *cis–trans* ratio of these fractions determined by argentation chromatography is in agreement with the previous infrared analyses. The *cis*- and *trans*-monoenes from linolenate reduced with hydridochlorobis(triphenylphosphine)platinum(II) and stannous chloride (Figure 2A) have the double-bond distributed between the 4 and 15 positions with the maximum at the 10 and 11 positions. The corresponding monoene from linolenate reduced with chloroplatinic acid and stannous chloride shows a double-bond distribution varying according to the hydrogenation temperature. In the monoenes from linolenate reduced at 65°, the double bond is distributed between the 5 and 15 positions (Figure 2B). The *cis* isomers, however, show maxima at the 9 and 15 positions, whereas the *trans* isomers have a bell-shaped distribution with maximum at the 10 position. With linolenate reduced at 100°, the double bond in both *cis* and *trans* monoenes is scattered between the 4 and 16 positions with the maximum at the 9 position. When hydrogenation is carried out at 65°, the double bond is less scrambled in the *cis*-monoene isomers and the 12 double bond is more reduced than the 9 and 15 double bonds of methyl linolenate.

The diene fraction from linolenate reduced with chloroplatinic acid–stannous chloride was further separated by preparative glpc (Figure 3). The unconjugated diene exhibited a partially resolved triple peak; the conjugated diene was resolved into the *cis,trans* and *trans,trans* isomers. The unconjugated diene was separated into the indicated fractions 1 and 3. Analytical glpc showed one peak for each of these isolated fractions. The intermediate fraction between 1 and 3 could not be isolated pure. Its retention time, however, corresponded to that of methyl linoleate. The double-bond distribution in diene fractions determined by ozonolysis–glpc is given in Figure 4. Diene fraction 1 had 147% *trans* and double bonds centered on the 9 and 14 positions. Diene fraction 3 had 88% *trans* and double bonds centered in the 8, 9, and 13 positions. Fraction 1 is the major unconjugated diene component and seems to be the product from linolenate in which the middle 12 double bond has been predominantly reduced. Fraction 3 is a minor isomeric diene in which

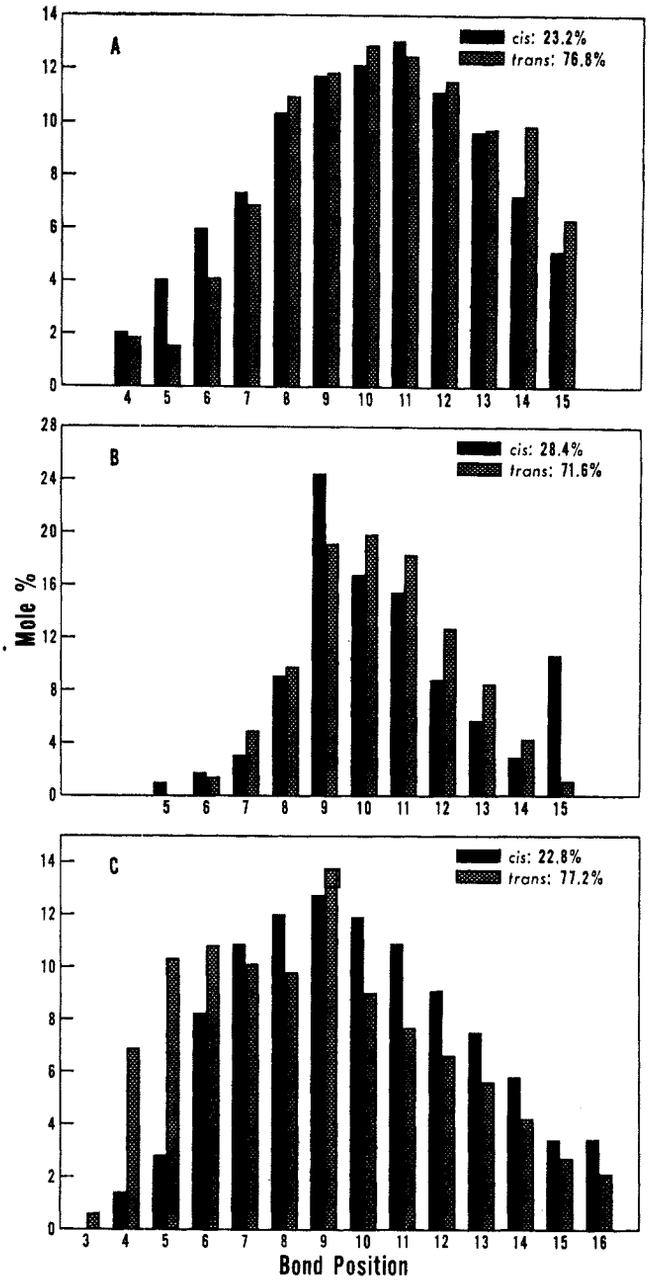

Figure 2.—Double-bond distribution in monoene fractions of hydrogenated methyl linolenate: A, hydridochlorobis(triphenylphosphine)platinum(II) + stannous chloride, run 1, Figure 1; B, chloroplatinic + stannous chloride, 65°, run 5, Table IA; and C, chloroplatinic acid + stannous chloride, 100°, run 8, Table IA.

the terminal 15 double bond of linolenate has been principally reduced.

Discussion

The homogeneous hydrogenation of methyl linolenate catalyzed by various platinum–tin chloride complexes is accompanied by extensive conjugation, *cis,trans* isomerization, and double-bond migration. The relative activity of these catalysts toward hydrogenation is in the following order: chloroplatinic acid + stannous chloride > dichlorobis(triphenylarsine)platinum(II) + stannous chloride > hydridochlorobis(triphenylphosphine)platinum(II) + stannous chloride > trichlorotin–hydridobis(triphenylphosphine)platinum(II). The first member of this series, on the one hand, is highly

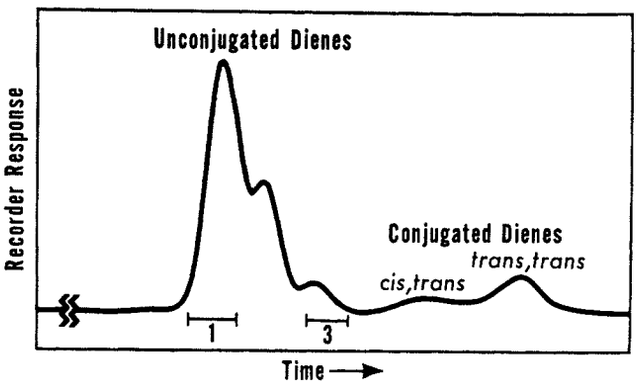

Figure 3.—Preparative glpc separation of diene fraction (chloroplatinic acid + stannous chloride, 65°, run 5, Table IA).

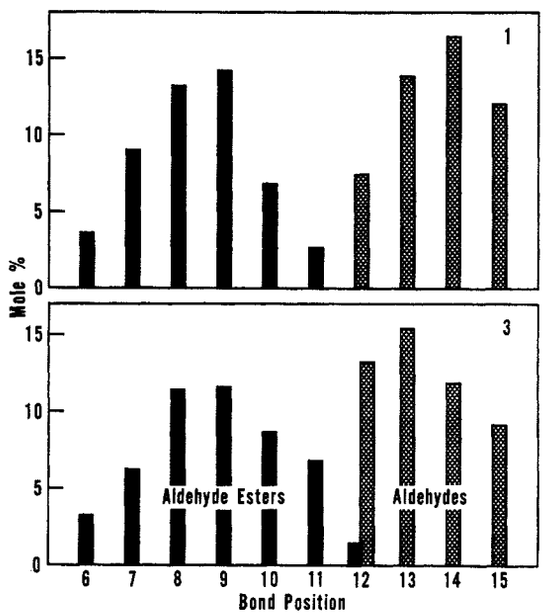

Figure 4.—Double-bond distribution in unconjugated diene fractions 1 and 3 (see Figure 3).

selective for the formation of diene from linolenate. The last member, on the other hand, promoted extensively the conjugation of methyl linolenate. Some of the structural factors[6] that may account for the differences in activity of these complexes include (a) relative basicity of the ligands, H, $(C_6H_5)_3P$, $(C_6H_5)_3As$, and $SnCl_3$; (b) steric effects; and (c) formation of different species with H_2PtCl_x and $(SnCl_3)_y$. Some of these factors would be expected to influence the lability of the Pt–H bond[7] in the hydrido complexes formed as intermediates during homogeneous hydrogenation.[5,6] The reason that methanol accelerates conjugation and facilitates hydrogenation of linolenate may be due to solubility effects, to its ability to convert transition metal complexes into hydrides,[8,9] and to its stabilizing effect on the complex trichlorotin–hydridobis(triphenylphosphine)platinum(II).[6] The activating effect of methanol is analogous to that observed previously with metal acetylacetonates.[3a] In this case, methanol was essential for hydrogenation and caused transesterification of triglycerides.

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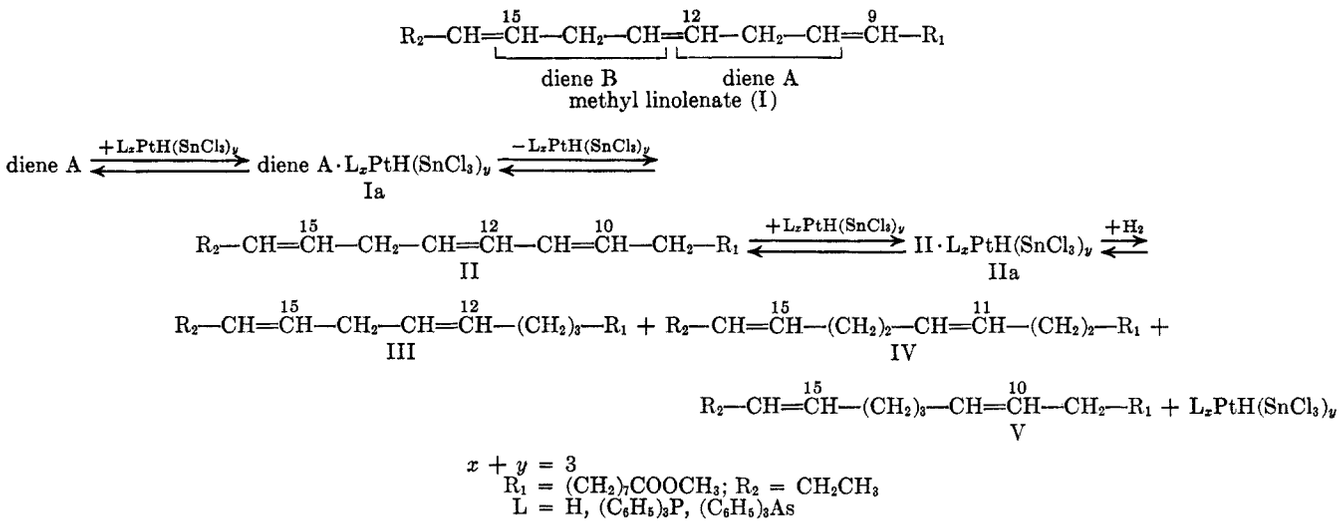
SCHEME I



Cramer, *et al.*,[10] have isolated the pentacoordinated platinum complex $[Pt(SnCl_3)_5]^{-3}$ which was shown by X-ray diffraction to have a trigonal bipyramid configuration. However, other workers[11,12] have obtained evidence for more than one species from mixtures of platinum(II) and tin(II) chlorides. From such mixtures, Lindsey, *et al.*,[13a] also obtained a complex anion, $[Pt_3Sn_8Cl_{20}]^{-4}$, formulated as a derivative of a Pt_3Sn_2 metal cluster. The acceleration of Zeise's salt formation by stannous chloride has been attributed[4] to the ability of stannous chloride to promote the coordination of ethylene to platinum. The ligand $SnCl_3^-$ exhibits a strong *trans* effect[13b,14] and this property which renders the H atom in Pt–H more hydridic[15] has been related[13b] to the catalytic activity of the platinum–tin chloride complexes. Bailar and Itatani[16] also attributed the catalytic properties of these complexes to their more ionic hydrido group resulting from the shift of electrons from the tin to the platinum.

A reaction pathway may be postulated for the homogeneous hydrogenation of methyl linolenate by platinum–tin complexes based on our evidence that (a) conjugated dienetrienes and conjugated trienes are important initial products; (b) double-bond migration occurs; (c) initially the middle 12 double bond is more reduced than the 9 and 15 double bonds of linolenate (the resulting dines have a high proportion of isomers with double bonds separated by several methylene groups); and (d) the platinum–tin catalysts form complexes with conjugated dienes such as isoprene.[16] The reaction sequence suggested (Scheme I) is similar to a previous one that we advanced for the homogeneous hydrogenation of linolenate catalyzed by iron pentacarbonyl.[3b] Diene conjugation occurs by the formation of an intermediate platinum–tin–diene complex on either the 9,12 or the 12,15 system of linolenate proposed previously for methyl linoleate.[5] Scheme I involves complex formation between the hydridoplatinum–tin chloride and the 9,12-diene system A of methyl linolenate. Conjugation is followed by intramolecular hydrogen exchange to convert the 1,4,7-triene (I) into a 1,3,6-conjugated dienetriene (II) as intermediate. Hydrogenation of II proceeds by addition of the trichlorotin–hydridoplatinum complex to the 1,3-diene system. The products include a 1,4-diene (III), a 1,5-diene (IV), and a 1,6-diene (V). Dienes IV and V are not conjugatable with alkali. They would be less susceptible to reduction *in a mixture with diene III*[17] because conjugation by the $HPtSnCl_3$ complex would require moving the double bond by several positions. Unreactive dienes of the types IV and V are indeed found to accumulate in partially hydrogenated methyl linolenate.[18] The reactive 1,4-diene III is conjugated by the same process as I. The resulting 1,3-dienes are hydrogenated into a mixture of isomeric *cis*- and *trans*-monoenes.

Extension of this scheme to both diene systems A and B of I leads to the formation of conjugated dienetrienes and conjugated trienes.[3b] The monoene products would show a double-bond distribution between the 8 and 16 positions. Further isomerization *via* conjugation followed by hydrogenation cannot occur past the 16,17 position of linolenate because of the terminal methyl group. Therefore, any additional isomerization is directed to the other side of the molecule down to the 4 and 5 positions. According to the proposed scheme, the middle 12 double bond of linolenate being involved in both conjugatable diene systems A and B is more susceptible to hydrogenation than the 9 and 15 double bonds. The accumulation of unreactive dienes with double bonds separated by several methylene groups thus accounts for the high selectivity of the platinum–tin chloride catalysts for the formation of dienes.

The two most important mechanisms currently discussed in the field of homogeneous catalytic hydrogena-

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(16) J. C. Bailar, Jr., and H. Itatani, *Inorg. Chem.*, **4**, 1618 (1965).

(17) Pure methyl *cis,cis*-9,15-octadecadienoate was readily hydrogenated with chloroplatinic acid and stannous chloride and the isomeric monoene products were similar to those of methyl linolenate (unpublished work). Therefore, it would appear that in a mixture of dienes competition exists and III is more readily hydrogenated than IV and V.

(18) See analyses of diene fractions in Table II and, also, Figure 4.

tion and isomerization of olefins by metal complexes[19,20] involve equilibria (a) between π-olefinic and σ-alkyl complexes and (b) through π-allylic complexes. The isomerization of pent-1-ene by a platinum–tin chloride complex was postulated[21] to involve the addition of the olefin to the hydride complex $[PtCl_x(SnCl_3)_{3-x}H]^{2-}$ (x = 0–2) to form the ion $[PtCl_x(SnCl_3)_{3-x}$ alkyl]. Isomerization would result from reversal of this step, whereas hydrogenation is caused by further reaction with hydrogen with regeneration of the complex hydride ion. A clear insight into the mechanism of complex formation, double-bond isomerization, and hydrogenation with platinum–tin chloride catalysts is not possible until the structure of organometallic intermediates involved in Scheme I can be elucidated and their stoichiometry established.

Experimental Section

Materials.—The preparation and some properties of the hydriodochlorobis(triphenylphosphine)platinum(II), $[(C_6H_5)_3P]_2PtHCl$, and the 1:1 adduct with stannous chloride have been described.[16] Dichlorobis(triphenylarsine)platinum(II), $[(C_6H_5)_3As]_2PtCl_2$, was made by a published procedure.[22] Methyl linolenate was separated from linseed esters by counter double current distribution between *n*-hexane and acetonitrile.[23] Glpc showed 100% triene; infrared showed no isolated *trans*. Conjugated dienes used as standard for glpc were derived from alkali conjugated methyl linoleate and conjugated dienetrienes and conjugated trienes from alkali-conjugated linseed methyl esters.[3e]

Hydrogenation.—Pressure hydrogenations were carried out in a solution of 40% methanol and 60% benzene (v/v) stirred in a Magne-Dash[24] 150-ml, stainless steel autoclave adapted with sampling tube.

Atmospheric hydrogenations were done in methanol solution stirred magnetically in a 50-ml erlenmeyer flask connected to a manometric system under 1 atmosphere hydrogen. Solvent was removed from the hydrogenated products under vacuum on a rotating evaporator. All products were redissolved in petroleum ether treated repeatedly with hydrochloric acid (1:1) to decompose the catalysts, then washed with water once, followed by saturated $NaHCO_3$, and then with water again to neutrality. The solution was dried over sodium sulfate.

Analyses.—Methods for glpc, infrared and ultraviolet spectroscopy, and alkali conjugation were the same as those used previously.[3d,e] Hydrogenation products were separated into monoene, diene, and triene fractions by countercurrent distribution between *n*-hexane and acetonitrile.[25] Monoene fractions were further resolved into *cis* and *trans* isomers by chromatography through a silver-saturated ion-exchange resin column.[26] Dienes were fractionated into nonconjugated isomers by preparative glpc according to a procedure already described.[3c] Position of double bonds was determined in the monoene fractions by potassium permanganate–potassium periodate oxidative cleavage[27] and in the diene fractions by ozonolysis–glpc.[28]

Registry No.—Methyl linolenate, 301-00-8; stannous chloride, 7772-99-8.

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Bishomofolic Acid. A New Synthesis of Folic Acid Analogs[1]

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Bishomofolic acid, a folic acid analog where the pteridine and aminobenzoyl groups are joined by three methylenes instead of one, has been synthesized. 5-Bromo-1-pentene and ethyl *p*-tosylamidobenzoate afforded 5-(*p*-carbethoxy-N-tosylanilino)-1-pentene (**3a**). The olefin was converted, through the epoxide, azido alcohol, and azido ketone, to an amino ketone hydrochloride, which as its semicarbazone (**8a**) was condensed with 2-amino-6-chloro-4-hydroxy-5-nitropyrimidine (**10**). The ketone function was regenerated and reductively cyclized with the nitrofunction to form the dihydropteridine. Oxidation afforded the N^{12}-tosylbishomopteroic ester; the 2-N-acetyl-N^{12}-tosyl acid was coupled with diethyl glutamate. The product was treated with base and detosylated with hydrogen bromide–acetic acid to form bishomofolic acid. The sequence was equally applicable to homofolic acid.

Homologs of folic acid with additional methylene groups inserted between the pteridine and aminobenzoyl groups represent an important modification of this important cofactor, but their synthesis constitutes a chemical problem beset with considerable practical difficulties. Homofolic acid (**20c**, which has one additional methylene) was synthesized recently,[2] and its tetrahydro derivative (A, n = 2) showed interesting activity in several biological systems.[3] Conceivably, this activity involved the formation of six-membered cyclic intermediates (B and C, n = 2) with one-carbon fragments, analogous to the five-membered cyclic intermediates formed by tetrahydrofolic acid (A, n = 1) in its function as a one-carbon transfer agent.[4] It was seen that the importance and the geometrical requirements of such intermediates might be tested with the next higher homolog, the so called "bishomofolic" acid (**20a**) having a third methylene, since unfavored seven-

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